Complete Summary

GUIDELINE TITLE

Multiple myeloma (MM).

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Multiple myeloma (MM). Helsinki, Finland: Duodecim Medical Publications Ltd.; 2001 Dec 27. Various p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Multiple myeloma (MM)

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Oncology

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collects, summarizes, and updates the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

- Patients with multiple myeloma (MM)
- Patients requiring evaluation for possible multiple myeloma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Assessment of clinical picture
2. Measures to distinguish between early cases of multiple myeloma (MM) and non-myeloma paraproteinaemias, especially monoclonal gammopathy with undetermined significance (MGUS).
3. Evaluation for marrow infiltration by plasma cells (>30%), lytic bone lesions, monoclonal protein in serum (>35 g/L IgG; >20 g/L IgA) and/or urine (>1 g/24 hours).
4. Basic examinations: bone marrow examination; serum and urine protein electrophoresis
5. Additional investigations when multiple myeloma is likely:
    - X-ray (skull, thorax/ribs, backbone, scapulae, pelvis and long bones of the extremities)
    - Serum/plasma total protein, albumin, potassium, sodium, calcium, ionised calcium, creatinine, urate and immunoglobulins (IgG, IgA, IgM)
    - Identification of M component heavy and light chains by immunofixation or by other means

Treatment; Management

1. No chemotherapy in symptomless patient
2. Symptomatic treatment
3. Supportive therapy
4. Maintenance of fluid and electrolyte balance
5. Treatment of hypercalcaemia
6. Treatment of infections
7. Maintenance of mobility in order to prevent osteoporosis and pathological fractures
8. Bisphosphonates (to treat hypercalcaemia and to prevent fractures)
9. Chemotherapy:
    - Initial therapy with melphalan (cyclophosphamide) and predniso(lo)ne
    - Refractory cases: vincristine, doxorubicin, and dexamethasone (VAD) or similar combinations; high-dose melphalan
    - Interferon
10. High-dose therapy and stem cell transplantation (autologous or rarely allogeneic) as indicated
11. Follow-up, including assessment of:
    - the amount of M component (serum and/or urine)
    - general condition and symptoms, infections and (bone) pains
    - osteolytic lesions (X-ray)

- renal function, hypercalcaemia and blood picture

MAJOR OUTCOMES CONSIDERED

- Signs and symptoms of multiple myeloma
- Complications of multiple myeloma, including pathological vertebral fractures
- Survival (lifetime and progression-free)
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A: Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.

B: Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.

C: Limited research-based evidence. At least one adequate scientific study.

D: No scientific evidence. Expert panel evaluation of other information.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Aim

- Early diagnosis is important, especially in order to prevent irreversible kidney lesions.

Pathology

- Multiple myeloma (MM) is a clonal haematopoietic malignancy in which malignant plasma cells accumulate in the bone marrow and produce an immunoglobulin, usually monoclonal IgG or IgA (an M component).
- Common complications include recurrent bacterial infections, anaemia, osteolytic lesions, and renal insufficiency.
- Monoclonal gammopathy with undetermined significance (MGUS) is marked by the presence in the serum of monoclonal IgG or IgA without evidence of

MM. Some of these patients (as many as 16% during a 30-year or longer follow-up period) develop MM. It is evident, however, that this outcome is less frequent among healthy individuals with an M component, the condition preferentially called benign paraproteinaemia. Only < 1% of these subjects develop MM.

Epidemiology

- Approximately 2-3 new cases/100,000/year.
- Diagnosis is usually made at the age of 50-70 years; rarely under the age of 40 years.
- No sex differences.

Aetiology

- In individual patients it remains unknown.
- Ionising irradiation slightly increases the risk.

Diagnosis

- The main diagnostic difficulty is to make a distinction between early cases of MM and non-myeloma paraproteinaemias, especially MGUS.
- The diagnosis of MM depends on finding:
    - marrow infiltration by plasma cells (> 30%)
    - lytic bone lesions
    - monoclonal protein in serum (>35 g/L IgG; >20 g/L IgA) and/or urine (>1 g/24 hours).

Differential Diagnostics

- In most cases of MGUS:
    - No symptoms and signs
    - No lytic bone lesions
    - Bone marrow plasmacytosis < 10%
    - M component smaller than in MM; IgG <30 g/L, IgA <10 g/L, urine protein <1 g/24 hours
    - Polyclonal immunoglobulins normal
- Waldenström's macroglobulinaemia (Bataille & Harousseau, 1997)
- Lymphomas with an M component
- Other rare diseases where there is an M component

Clinical Picture

- Often:
    - Osteolytic lesions and bone pains
    - Mild-to-moderate anaemia, hypercalcaemia, hyperuricaemia
    - Renal insufficiency
- Rarely:
    - Hyperviscosity syndrome (IgA myeloma)

Typical Laboratory Findings

- Increased erythrocyte sedimentation rate (ESR) (not in light-chain myeloma)
- M component in serum and/or urine
- Decreased haemoglobin level, often also leuco- and thrombocytopenia
- Malignant plasma cell infiltrates in the bone marrow
- Osteolytic lesion in bone X-ray (magnetic imaging may be more sensitive)
- Often increased serum urate and calcium but diminished albumin concentration

Basic Examinations

- Bone marrow examination
- Serum and urine protein electrophoresis (M component can be found in urine in only 10-20% of MM patients)

Additional Investigations when MM is Likely

- X-ray (skull, thorax/ribs, backbone, scapulae, pelvis and long bones of the extremities)
- Serum/plasma total protein, albumin, potassium, sodium, calcium, ionised calcium, creatinine, urate and immunoglobulins (IgG, IgA, IgM)
- Identification of M component heavy and light chains by immunofixation or by other means

Complications

- Renal insufficiency
- Pathological bone fractures
- Hypercalcaemia
- Hyperviscosity syndrome rarely (mostly in IgA myeloma)
- Amyloidosis as a late complication
- Sometimes plasma cell leukaemia, myelodysplastic syndrome or acute leukaemia

Disease Progression and Prognosis

- Median life expectancy at diagnosis is about 3.5-4 years. Marked individual variation exists.
- Myeloma cell infiltrates occupy the bone marrow causing anaemia as well as leuco- and thrombocytopenia.
- Myeloma cells become gradually resistant to chemotherapy.
- Infections, haemorrhages and renal insufficiency are frequent complications.

Follow-up and Treatment

- If the patient is symptomless, no chemotherapy will be given.
- Treatment is given actively to relieve symptoms.

In Follow-up, Attention is Paid to:

- The amount of M component (serum and/or urine)
- General condition and symptoms, infections and (bone) pains

- Osteolytic lesions (X-ray)
- Renal function, hypercalcaemia and blood picture.

Supportive Therapy Includes:

- Maintenance of fluid and electrolyte balance
- Treatment of hypercalcaemia
- Treatment of infections
- Maintenance of mobility in order to prevent osteoporosis and pathological fractures
- Bisphosphonates (to treat hypercalcaemia and to prevent fractures) (Djulbegovic et al., 2002) [A]

Chemotherapy

- According to instructions given by a specialist
- Melphalan (cyclophosphamide) and predniso(lo)ne are used for the initial therapy
- Refractory cases
    - Vincristine, doxorubicin, and dexamethasone (VAD) or similar combinations
    - High-dose melphalan
- Interferon may be tried, but benefit is uncertain (Trippoli et al., 1997; DARE, 1999) [B]

High-dose Therapy and Stem Cell Transplantation

- Autologous transplantation is considered for most patients (who appear to tolerate high-dose chemotherapy) under the age of 65-70 years (Johnson et al., 1998; DARE, 2000) [C].
- Rarely, allogeneic stem cell transplantation.

Definitions:

Levels of Evidence

A: Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.

B: Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.

C: Limited research-based evidence. At least one adequate scientific study.

D: No scientific evidence. Expert panel evaluation of other information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Reduction of symptoms and prevention of complications through early diagnosis and treatment

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Multiple myeloma (MM). Helsinki, Finland: Duodecim Medical Publications Ltd.; 2001 Dec 27. Various p.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Dec 27

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Juhani Vilpo

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: The following formats are available:

- HTML
- Portable Document Format (PDF)
- ASCII Text

This guideline is also included in a CDROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

- EBM guidelines. Evidence-based medicine. Helsinki, Finland: Duodecim Medical Publications, Ltd. 2002. [CDROM]
- EBM guidelines. Web site: www.ebm-guidelines.com.

Available from: Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer as of February 7, 2003.

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